

COMPOSITIONS AND METHODS FOR TREATING BRAIN-GUT DISORDERS

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application No. 62/714,468, filed Aug. 3, 2018; U.S. Provisional Application No. 62/714,470, filed Aug. 3, 2018; U.S. Provisional Application No. 62/720,453, filed Aug. 21, 2018; U.S. Provisional Application No. 62/732,753, filed Sep. 18, 2018; U.S. Provisional Application No. 62/789,502, filed Jan. 7, 2019; U.S. Provisional Application No. 62/789,438, filed Jan. 7, 2019; U.S. Provisional Application No. 62/789,470, filed Jan. 7, 2019; U.S. Provisional Application No. 62/789,492, filed Jan. 7, 2019; U.S. Provisional Application No. 62/789,496, filed Jan. 7, 2019; U.S. Provisional Application No. 62/789,468, filed Jan. 7, 2019; U.S. Provisional Application No. 62/789,439, filed Jan. 7, 2019; U.S. Provisional Application No. 62/789,478, filed Jan. 7, 2019; U.S. Provisional Application No. 62/789,481, filed Jan. 7, 2019; and U.S. Provisional Application No. 62/789,441, filed Jan. 7, 2019, the contents of which are incorporated herein by reference in their entirety.

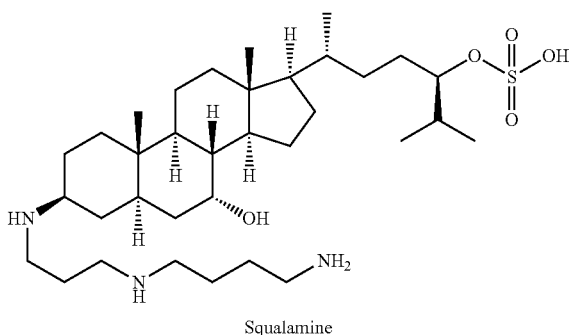
FIELD

[0002] The present application relates generally to compositions and methods for treating and/or preventing a variety of symptoms and disorders related thereto with aminosterols or pharmaceutically acceptable salts or derivatives thereof.

BACKGROUND

[0003] Aminosterols are amino derivatives of a sterol. Examples of aminosterols include squalamine and Aminosterol 1436 (also known as trodusquemine and MSI-1436).

[0004] Squalamine is a unique compound with a structure of a bile acid coupled to a polyamine (spermidine):



[0005] The discovery of squalamine, the structure of which is shown above, was reported by Michael Zasloff in 1993 (U.S. Pat. No. 5,192,756). Squalamine was discovered in various tissues of the dogfish shark (*Squalus acanthias*) in a search for antibacterial agents. The most abundant source of squalamine is in the livers of *Squalus acanthias*, although it is found in other sources, such as lampreys (Yun et al., 2007).

[0006] Several clinical trials have been conducted relating to the use of squalamine, including the following:

[0007] (1) ClinicalTrials.gov Identifier NCT01769183 for "Squalamine for the Treatment in Proliferative Diabetic Retinopathy," by Elman Retina Group (6 participants; study completed August 2014);

[0008] (2) ClinicalTrials.gov Identifier NCT02727881 for "Efficacy and Safety Study of Squalamine Ophthalmic Solution in Subjects With Neovascular AMD (MAKO)," by Ohr Pharmaceutical Inc. (230 participants; study completed December 2017);

[0009] (3) ClinicalTrials.gov Identifier NCT02614937 for "Study of Squalamine Lactate for the Treatment of Macular Edema Related to Retinal Vein Occlusion," by Ohr Pharmaceutical Inc. (20 participants; study completed December 2014);

[0010] (4) ClinicalTrials.gov Identifier NCT01678963 for "Efficacy and Safety of Squalamine Lactate Eye Drops in Subjects With Neovascular (Wet) Age-related Macular Degeneration (AMD)," by Ohr Pharmaceutical Inc. (142 participants; study completed March 2015);

[0011] (5) ClinicalTrials.gov Identifier NCT00333476 for "A Study of MSI-1256F (Squalamine Lactate) To Treat "Wet" Age-Related Macular Degeneration," by Genaera Corporation (140 participants; study terminated);

[0012] (6) ClinicalTrials.gov Identifier NCT00094120 for "MSI-1256F (Squalamine Lactate) in Combination With Verteporfin in Patients With "Wet" Age-Related Macular Degeneration (AMD)," by Genaera Corporation (60 participants; study completed February 2007); and

[0013] (7) ClinicalTrials.gov Identifier NCT00089830 for "A Safety and Efficacy Study of MSI-1256F (Squalamine Lactate) To Treat "Wet" Age-Related Macular Degeneration," by Genaera Corporation (120 participants; study completed May 2007).

[0014] Aminosterol 1436 is an aminosterol isolated from the dogfish shark, which is structurally related to squalamine (U.S. Pat. No. 5,840,936). It is also known as MSI-1436, trodusquemine and produlestan.

[0015] Several clinical trials have been conducted relating to the use of Aminosterol 1436:

[0016] (1) ClinicalTrials.gov Identifier NCT00509132 for "A Phase I, Double-Blind, Randomized, Placebo-Controlled Ascending IV Single-Dose Tolerance and Pharmacokinetic Study of Trodusquemine in Healthy Volunteers," by Genaera Corp.;

[0017] (2) ClinicalTrials.gov Identifier NCT00606112 for "A Single Dose, Tolerance and Pharmacokinetic Study in Obese or Overweight Type 2 Diabetic Volunteer," by Genaera Corp.;

[0018] (3) ClinicalTrials.gov Identifier NCT00806338 for "An Ascending Multi-Dose, Tolerance and Pharmacokinetic Study in Obese or Overweight Type 2 Diabetic Volunteers," by Genaera Corp.;

[0019] (4) ClinicalTrials.gov Identifier: NCT02524951 for "Safety and Tolerability of MSI-1436C in Metastatic Breast Cancer," by DepyMed Inc.

[0020] Even in view of these trials, the full potential of aminosterols for use in treatment has yet to be determined.

SUMMARY

[0021] In a first embodiment, the disclosure relates to a method of treating, preventing, and/or slowing the onset or progression in a subject in need of a condition selected from